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"Real-time calculation of system-level complexity during trauma/hemorrhage: can we do it?"

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Objectives: We previously showed that sample entropy (SampEn), and other nonlinear measures of the complexity of the ECG time series, decrease in response to hypovolemia and/or injury. These measures characterize only one signal, and thus refer to *signal-level complexity*. In contrast, *system-level complexity* quantifies the amount of interaction among the signals arising from all available sensors attached to a patient (ECG, blood pressure, oxygen saturation, etc.). We found that system-level complexity (OSC) calculated with OntoSpace software (Ontonix S.r.l., Como, Italy) fluctuates during critical events such as asphyxia. Relatedly, *system robustness* (OSR) represents the margin between current OSC and maximal or minimal possible OSC. OSR thus is greatest when OSC is in the middle range; it decreases when OSC approaches either extreme, where the system becomes unstable and is prone to crash. Here, we present data calculated in real time from both signal-level and system-level complexity in a model of acute respiratory distress syndrome (ARDS) due to trauma, hemorrhagic shock and resuscitation. **Methods:** Nine swine were anesthetized with ketamine and midazolam and underwent baseline measurements (BL), right-chest pulmonary contusion (PC), hemorrhage of 12 mL/kg (Bleed), resuscitation with lactated Ringer's (LR), transfusion of shed blood (Tx), and post-resuscitation observation (Post-Resus). Data were collected continuously and analyzed in 15-min datasets. We calculated heart rate (HR, bpm); mean arterial pressure (MAP, mmHg); PaO_2-to-FiO_2 ratio (PFR); ECG SampEn (unitless); ECG multiscale entropy (MSE, unitless), and percentage of normal-to-normal RRIs differing by more than 50 ms (pNN_{50}). We calculated OSC and OSR (both unitless) from 56 different channels of single-sensor data. **Results:** see table. Means±SEMs are reported. Statistics: one way ANOVA with Tukey's adjustment.

	BL	PC	Bleed	LR	Tx	Post Resus
HR	80±5	101±5*	109±6*	115±12*	106±9*	104±7*
MAP	83±5	54±4*	58±6*	68±4*†	69±4*†	75±4†
PFR	479±9	198±29*	196±36*	162±36*	174±35*	246±39*¥≠°
SampEn	2.0±0.2	1.6±0.2*	1.5±0.1*	1.6±0.2	1.7±0.3	2.0±0.2¥
MSE	18.9±2.4	15.3±2.4	13.5±1.8	14.1±2.3	14.1±2.6*	16.8±2.4
PNN50	0.28±0.10	0.10±0.04	0.09±0.03	0.11±0.02	0.15±0.05	0.22±0.06†¥
OSC	3.6±0.5	20.0±1.9*	12.7±1.5*†	9.2±0.9*†¥	6.5±0.6*†¥	9.5±0.9*†¥≠
OSR	93.5±0.3	61.1±1.3*	78.5±0.9*†	82.9±0.6*†	88.7±0.32†°	83.2±0.68*†≠

***Significant ($p<0.05$) vs.BL; †vs. PC; ¥vs. Bleed; °vs. LR; ≠vs. Tx.

Conclusions: Measures of signal-level complexity like SampEn, and measures of system-level complexity like OSC, address fundamentally different characteristics of a patient's physiology. This is the first report containing data acquired in real-time and combining both approaches in a model of ARDS caused by trauma/hemorrhage. Future work will address whether this combined approach to monitoring can be used to improve outcomes in critical care by enabling earlier or more effective intervention in potentially unstable patients.